REMARKS

Claims 1 -14 are currently amended. Claim 15 has been added. Accordingly, claims 1 -15 are presently pending in this application.

Claims 4, and 8-12 stand rejected under 35 U.S.C § 112, second paragraph, as being allegedly indefinite for failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office rejects claim 4 for recitation of "as chloride salts". Claim 4 has been amended to delete this phrase.

The Office rejects claim 8 for recitation of "thiamine pyrophosphate chloride", but claim 8 depends from claim 1 which recites "cocarboxylase". Claim 1 has been amended to recite "thiamine pyrophosphate" in lieu of "cocarboxylase". Claim 8 has been amended to delete "chloride". Thiamine pyrophosphate is the equivalent of cocarboxylase, and chloride is merely one salt form of the thiamine pyrophosphate.

The Office rejects claim 9 for incorrect recitation of "gmoles/L". Claim 9 has been amended to recite "μmoles/L" in lieu of "gmoles/L".

The Office rejects claim 10 for recitation of "(expressed in E. coli)". Claim 10 has been amended to delete this phrase, and claim 15 has been added to further limit the recombinant human insulin to that which derived from expression in *E. coli.*

The Office rejects claim 11 for misspelling dichloroacetamide. This term has been corrected as suggested by the Office.

The Office rejects claim 12, which depends from claim 1, for recitation of "thiamine". Claim 12 has been amended to recite "thiamine pyrophosphate".

The Office further suggests amending claim 1 to include a comma between glucose and glycerol and a comma between glutamate and aspartate, to remove "; and" and to end claim 1 with a period. The dependent claims should start with "The". Claim 2 should state "which further comprises". Claim 1, 2 and the other dependent claims have been amended to incorporate all of the Office's suggestions.

Accordingly, all of the rejected claims have been amended to address the Office's rejections and suggestions. Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 1, 3-10 and 12-14 stand rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Parr *et al.* in view of Clements *et al.* Specifically, the Office alleges that it would have been obvious to substitute the concentration of TTP taught in Clements for the amount used in the solution taught in Parr, thereby obtaining the presently claimed solution.

Applicant respectfully traverses the Office's rejection. To establish a *prima facie* case of obviousness, there must be 1) a suggestion to combine or modify, 2) a reasonable expectation of success and 3) the references must suggest all of the claim limitations. MPEP § 2143. According to *Perkin-Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 894 (Fed. Cir. 1984), "the critical question, as § 103 makes plain, is whether the invention as a whole would have been obvious to one of ordinary skill in the art at the time it was made". It is improper to compare the prior art with the "gist" of the invention. *Jones v. Hardy,* 727 F.2d 1524, 1527-28 (Fed. Cir. 1984). It is essential, therefore, to consider all elements of the claimed invention.

First, Parr taught a composition for perfusing rat tissue. Clements taught a composition for perfusing fish tissue. Because the compositions were designed to perfuse the tissues of different types of animals, the two composition differ substantially, especially in their

salt component (i), buffer component (ii), and co-enzyme component (v). Given that there are 7 components in claim 1 of the present application and over 15 components in the compositions (as presented in the tables) of the cited references, it would not have been obvious, without undue experimentation, to determine which components to modify to reach the claimed solution. There is no suggestion or motivation to modify the cited references. Nothing in either cited references suggests that their compositions were inferior and therefore, needing improvements, especially with any particular component.

Second, Parr's composition consists of, among other components, 0.043 mmol/L of TTP or deoxythymidine 5'-triphosphate. TTP is different from TPP, which is thiamine pyrophosphate. Therefore, Parr's solution does not contain thiamine cocarboxylase/TPP, which is a required element of claim 1 of the present application. Several de-phosphorylation steps would be necessary to convert TTP to TPP.

The Office further alleges that the DL-carnitine in Parr can reasonably be substituted for L-carnitine of claim 9 of the present application. However, as Applicant stated at p. 7 of the specification, lines 15-31, the "L-carnitine is preferred to the D- or DL-isomers, because it causes no inhibition of acetyl co-enzyme A/free fatty acid metabolism." Moreover, it is known in the art that optical isomers of organic compounds can behave biologically different. A mixture of forms (DL) cannot be reasonably assumed to behave equivalently to the pure form.

Applicant submits that it is improper to use hindsight, using the teachings of the present application, to construct the claimed solution from the cited references. In order to achieve the claimed solution, a person of ordinary skill in the art would have to make several modifications. For example, he would have to change the component from TTP to TPP, then to reduce the TPP by a thousand fold, and also to replace DL-carnitine with L-carnitine.

The Office also alleges that Parr's 25 ml U/L of porcine insulin would be functionally equivalent to 28 ml U/L of recombinant human insulin in claim 10. Claim 10 depends from claim 1, and thus, contains all of the limitations of claim 1. Applicant reasserts the above argument to this rejection of claim 10. A person of ordinary skill in the art would have to extensively modify the compositions in the cited references to achieve the claimed solution. For example, the skilled artisan would have to change the component from TTP to TPP, then to reduce the TPP by a thousand fold, and also to replace DL-carnitine with L-carnitine. This would require undue experimentation and thus, would not have been obvious to such a skilled artisan. In addition, claim 10 calls for a recombinant human insulin. A recombinant insulin provides advantages to natural insulin in that a recombinant insulin has a lower tendency for undesirable antigen contaminants.

The Office further alleges that the subject matter of claim 12 would have been obvious to a skilled artisan because it merely recites a particular order of mixing. Claim 12 depends from claim 1, and thus, contains all of the limitations of claim 1. Applicant reasserts the above argument to this rejection of claim 12. A person of ordinary skill in the art would have to extensively modify the compositions in the cited references to achieve the claimed solution. For example, the skilled artisan would have to change the component from TTP to TPP, then to reduce the TPP by a thousand fold, and also to replace DL-carnitine with L-carnitine. This would require undue experimentation and thus, would not have been obvious to such a skilled artisan. In addition, the order of mixing in claim 12 provides advantages. For example, the insulin is added after BES to maintain an acid pH. An acidic environment prevents the insulin from forming polymer aggregates.

Claims 13 and 14 stand rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Parr *et al.* and Clements *et al.*, further in view of the Gibco catalog.

Claims 13 and 14 depend from claim 1, and thus, contain all of the limitations of claim 1. Applicant reasserts the above argument to this rejection of claims 13 and 14. A person of ordinary skill in the art would have to extensively modify the compositions in the cited references to achieve the claimed solution. For example, the skilled artisan would have to change the component from TTP to TPP, then to reduce the TPP by a thousand fold, and also to replace DL-carnitine with L-carnitine. This would require undue experimentation and thus, would not have been obvious to such a skilled artisan.

Claims 2 and 11 stand rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Parr *et al.* and Clements *et al.*, further in view of Rees *et al.*

Claims 2 and 11 depend from claim 1, and thus, contain all of the limitations of claim 1. Applicant reasserts the above argument to this rejection of claims 2 and 11. A person of ordinary skill in the art would have to extensively modify the compositions in the cited references to achieve the claimed solution. Regardless of the exact amount of chloramphenicol to use in the solution, to obtain the claimed solutions, the skilled artisan would have to, for example, change the component from TTP to TPP, then to reduce the TPP by a thousand fold, and also to replace DL-carnitine with L-carnitine. This would require undue experimentation and thus, would not have been obvious to such a skilled artisan.

Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant, therefore, respectfully requests that the Office reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Office believes, for any reason, that personal communication will expedite prosecution of this application, it is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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